Amendments to the Claims:

1. (Currently amended) A method of screening for an agent ~~to determine its usefulness in treating insulin resistance, the method comprising:~~

~~a) identifying proteins which are differentially expressed in biological samples obtained from insulin resistant, normal or insulin sensitive subjects in response to a known treatment or compound which alters insulin sensitivity~~

~~b) providing a biological sample comprising cellular tissue or a subcellular fraction thereof susceptible to insulin action;~~

~~c) contacting the sample of step b) with said agent and identifying proteins which are differentially expressed in response to said agent; and~~

~~d) comparing the results of a) and c) thereby identifying those agents which alter the expression levels of said proteins towards that observed in an insulin resistant or insulin sensitive subject.~~ having efficacy in treating insulin resistance, the method comprising:

a) providing

i) a first biological sample obtained from an insulin resistant subject,

ii) a second biological sample obtained from a normal or comparatively insulin-sensitive subject,

iii) a third biological sample obtained from an insulin resistant subject who has been treated with a known treatment or compound which alters insulin sensitivity, and

iv) a fourth biological sample obtained from a normal or comparatively insulin-sensitive subject who has been treated with said known treatment or compound;

b) identifying at least one differentially expressed protein which is:

(i) differentially expressed in said first and second biological samples;

(ii) differentially expressed in said first and third biological samples; and

(iii) not differentially expressed in said second and fourth biological samples; or differentially expressed in said second and fourth biological samples to a lesser degree than in said first and third biological samples;

c) providing a fifth biological sample comprising cellular tissue susceptible to insulin action or a subcellular fraction thereof obtained from an insulin resistant subject, wherein said fifth biological sample has been treated with said agent or said insulin resistant subject has been treated with said agent; and

d) determining the level of expression of said at least one differentially expressed protein in said fifth biological sample, agents which alter the expression level towards that observed in the second or third biological sample having efficacy for the treatment of insulin resistance.

2. (Currently amended) The method of claim 1, wherein the agent is selected if it ~~if~~ changes the expression of the at least one differentially expressed protein ~~or proteins~~ towards that of a normal subject or a more insulin sensitive subject.

3. (Currently amended) The method of claim 2, wherein the agent is selected if it converts the expression of the at least one differentially expressed protein ~~or proteins~~ to that of a normal or more insulin sensitive subject.

4. (Canceled)

5. (Currently amended) The method of claim 1, wherein the normal or comparatively insulin-sensitive subject~~s~~ of step a) ~~comprise~~ is a normal subject~~s~~ ~~and~~ or an abnormally insulin sensitive subject~~s~~.

6. (Currently amended) The method of claim 5, wherein the abnormally insulin sensitive subject~~s~~ ~~have~~ has acquired higher than normal sensitivity by exercise.

7. (Currently amended) The method of claim 1, wherein the ~~relevant~~ cellular tissue of the fifth biological sample is selected from the group consisting of liver, skeletal muscle, white or brown adipose tissue.

8-13. (Canceled)

14. (Currently amended) The method of claim 1, wherein the insulin-resistant subject~~s~~ of step a) ~~are~~ is an animal~~s~~ which ~~are~~ is insulin-resistant as a result of genetic mutation, and the normal or comparatively insulin-sensitive subject~~s~~ ~~are~~ is a normal control animal~~s~~.

15. (Currently amended) The method of claim 14, wherein the normal control animal~~s~~ ~~are~~ is an insulin sensitive littermate~~s~~ of the genetically mutated animal~~s~~.

16. (Currently amended) The method of claim 1, wherein the ~~test~~ insulin-resistant subject~~s~~ of step a) ~~are~~ is an animal~~s~~ which ~~are~~ is insulin-resistant as a result of diet, and the normal or comparatively insulin-sensitive subject~~s~~ ~~are~~ is a normal control animal~~s~~.

17. (Previously amended) The method of claim 1, wherein the normal and insulin resistant subjects of step a) are animals which are insulin-sensitive on a natural diet, but develop insulin resistance when given an unnatural, laboratory diet.

18. (Currently amended) The method of claim 1, wherein the treatment ~~to increase~~ which alters the level of insulin sensitivity comprises ~~treatment with~~ administration of an insulin-sensitising drug.

19. (Original) The method of claim 18, wherein the insulin sensitizing drug is thiazolidinedione.

20. (Original) The method of claim 19, wherein the thiazolidinedione is rosiglitazone (BRL 49653).

21. (Original) The method of claim 18, wherein the insulin sensitizing drug is a non-thiazolidinedione which is (a) an agonist or partial agonist of the PPAR gamma nuclear receptor, (b) a b3-adrenoceptor agonist or (c) a leptin or leptin fragment.

22. (Currently amended) The method of claim 1, wherein the treatment ~~to increase~~ which alters the level of insulin sensitivity comprises dietary restriction and/or exercise.

23. (Currently amended) The method of claim 1, wherein the fifth biological sample of step ~~b~~c) is taken from a subject suffering from non-insulin dependent diabetes.

24. (Currently amended) The method of claim 1, wherein the fifth biological sample of step ~~b~~c) is taken from a subject suffering

from polycystic ovary syndrome, syndrome X, insulin resistance syndrome or type I diabetes.

25. (Currently amended) The method of claim 1, wherein the differentially expressed proteins are identified by two-dimensional gel electrophoresis ~~carried out on the relevant tissue or a protein-containing extract thereof~~.

26. (Canceled)

27. (Currently amended) The method of claim 1, further comprising the step of isolating at least one of the differentially expressed proteins identified in the method.

28. (Original) The method of claim 27, further comprising the step of characterizing the isolated protein.

29. (Currently amended) The method of claim 1, wherein the at least one differentially expressed protein ~~or proteins~~ comprises one or more of LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30, MOM31, MOM32, MOM33, MOMT34, MOMT35, MOM36, WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64, WSEM65, BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77.

30. (Currently amended) The method of claim 28, further comprising ~~using the protein in an assay for~~ identifying specific binding partners of the isolated protein.

31. (Currently amended) The method of claim 28, further comprising ~~using the protein in an assay to~~ screening for agonists or antagonists of the isolated protein.

32. (Previously amended) The method of claim 1, wherein the agents or proteins are screened using a high throughput screening method.

33. (Currently amended) ~~A~~ The method of claim 1 further comprising preparation of ~~making~~ a pharmaceutical composition ~~which~~ comprise~~s~~ing ~~having~~ the identified ~~an~~ agent ~~using the method of claim 1, the further step of~~ , said method further comprising a) manufacturing the agent and b) formulating ~~it~~ the agent with an acceptable carrier ~~to provide the pharmaceutical composition~~.

34. (Withdrawn) A protein for use in a method of medical treatment, wherein the protein is selected from LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30, MOM31, MOM32, MOM33, MOMT34, MOMT35, MOM36, WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64, WSEM65, BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77

Claims 35-37 (Cancelled)

38. (Withdrawn) A method of treating a condition characterised by insulin resistance in a patient, the method comprising administering a therapeutically or prophylactically effective amount of such an agent identified by a method of claim 1 to the patient.

39. (Withdrawn) A method of determining the nature or degree of insulin resistance in a sample of relevant tissue from a human or animal subject, which comprises:

a) establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having differential levels of insulin sensitivity;

b) obtaining a sample of the tissue and

c) determining the presence, absence or degree of expression of the differentially expressed protein or proteins in the sample, and

d) relating the determination to the nature or degree of the insulin resistance by reference to a previous correlation between such a determination and clinical information.

40. (Withdrawn) The method of claim 39, wherein in the paradigm at least four protein are differentially expressed, providing a multi-protein finger print of the nature or degree of insulin resistance.

41. (Withdrawn) The method of claim 39, wherein in the paradigm the subjects having differential levels of insulin sensitivity comprise normal subjects and insulin resistant subjects.

42. (Withdrawn) The method of claim 39, wherein the subjects having differential levels of insulin sensitivity comprise normal subjects and subjects having abnormally high insulin sensitivity.

43. (Withdrawn) The method of claim 39, which further comprises determining an effective therapy for treating the abnormality.

44. (Withdrawn) The method of claim 39, wherein the sample is taken from a patient undergoing treatment for the insulin resistance and wherein the method further comprises monitoring the treatment.

45. (Withdrawn) A protein which is differentially expressed in relevant tissue from or representative of subjects having differential levels of insulin sensitivity and which is obtainable by the method of two-dimensional gel electrophoresis carried out on said tissue or a protein-containing extract thereof, the method comprising:

a) providing non-linear immobilized pH gradient (IPG) strips of acrylamide polymer 3 mm x 180 mm;

b) rehydrating the IPG strps in a cassette containing 25 ml. of an aqueous solution of urea (8M), 3- [(cholamidopropyl) dimethylammonio]-1-propanesulphonate (CHAPS, 2% w/v), dithioerythritol (DTE, lOmM), mixture of acids and bases of pH 3.5 to 10 (2% w/v) and a trace of Bromophenol Blue;

(c) emptying the cassette of liquid, transferring the strips to an electrophoretic tray fitted with humid electrode wicks, electrodes and sample cups, covering the strips and cups with low viscosity paraffin oil;

(d) applying 200 micrograms of an aqueous solution of dried, powdered material of the relevant body tissue in urea (8M), CHAPS (4% w/v), Tris (40 mM), DTE (65 mM), SDS (0.05% w/v) and a trace of Bromophenol Blue to the sample cups, at the cathodic end of the IPG strips;

(e) carrying out isoelectric focusing on the gel at a voltage which increases linearly from 300 to 3500 V during 3 hours, followed by another 3 hours at 3500 V, and thereafter at 5000V for a time effective to enable the proteins to migrate in the strips to their pI- dependent final positions;

(f) equilibrating the strips within the tray with 100 ml of an aqueous solution containing Tris-HCl (50 mM) pH 6.8, urea (6M), glycerol (30% v/v), SDS (2% w/v) and DTE (2% w/v) for 12 minutes;

(g) replacing this solution by 100 ml. of an aqueous solution containing Tris-HCl (50 mM) pH 6.8, urea (6M), glycerol (30% v/v), SDS (2% w/v), iodoacetamide (2.5% w/v) and a trace of Bromophenol Blue for 5 minutes ;

(h) providing a vertical gradient slab gel 160 x 200 x 1.5 mm of acrylamide/piperazine-diacrylyl cross- linker (9-16% T/2. 6% C), polymerised in the presence of TEMED (0.5% w/v), ammonium persulphate (0.1% w/v) and sodium thiosulphate (5 mM), in Tris-HCl (0.375M) pH 8.8 as leading buffer ;

(i) over-layering the gel with sec-butanol for about 2 hours, removing the overlay and replacing it with water;

(j) cutting the IPG gel strips to a size suitable for the second dimensional electrophoresis, removing 6 mm from the anode end and 14 mm from the cathode end; (k) over-layering the slab gel with an aqueous solution of agarose (0.5% w/v) and Tris-glycine-SDS (25 mM-198 mM-0.1% w/v) as leading buffer, heated to 70°C and loading the IPG gel strips onto the slab gel through this over-layered solution;

(l) running the second dimensional electrophoresis at a constant current of 40 mA at 8-12°C for 5 hours; and

(m) washing the gel.

46. (Withdrawn) A differentially expressed protein of claim 45 as obtainable from mouse liver cells of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30.

47. (Withdrawn) A differentially expressed protein of claim 45 as obtainable from skeletal muscle cells of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein MOM31, MOM32, MOM33, MOMT34, MOMT35 or MOM36.

48. (Withdrawn) A differentially expressed protein of claim 45 as obtainable from white adipose tissue of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64 or WSEM65.

49. (Withdrawn) A differentially expressed protein according to claim 45 as obtainable from brown adipose tissue of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77.

50. (Withdrawn) A differentially expressed protein having one or more of the identifying characteristics set out in Table 1 to 4.

51. (Withdrawn) The differentially expressed protein of claim 50, wherein the identifying characteristics are pI and Mw.

52. (Currently amended) ~~A~~ The method of claim 1, ~~whereby the pattern of differentially expressed proteins in~~ wherein said biological samples are ~~a~~ tissue samples or body fluid samples ~~of an individual with insulin resistance~~ said method further comprising the steps of:

f) ~~is used to~~ predicting the most appropriate and effective therapy to alleviate ~~the~~ insulin resistance; and

g) ~~to~~ monitoring the success of ~~that treatment~~ said therapy.

53. (Currently amended) The method of claim 1~~0~~, wherein the comparatively insulin sensitive subject~~s~~ ~~are~~ is a normal subject~~s~~ or an abnormally insulin sensitive subject~~s~~.